Mini Review
Volume 13:12, 2022

Journal of Molecular Biomarkers & Diagnosis

ISSN: 2155-9929 Open Access

Serum-based Stability of Circulating MicroRNAs

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Abstract

Our goal was to find novel protein associations that could serve as biomarkers for bipolar disorder that could be used in the real world. In order to accomplish this, we analyzed 201 distinct proteins found in blood serum from two distinct cohorts of patients with bipolar disorder and healthy controls using the proximity extension assay. After controlling for relevant covariates, we discovered 32 proteins that significantly correlated with bipolar disorder in both case-control cohorts. Despite the fact that ten proteins have previously been linked to bipolar disorder, twenty-two of these findings are novel to the disorder. Matrilysin, pro-adrenomedullin, chitinase-3-like protein 1, C-C motif chemokine 3, interleukin 10, growth/differentiation factor 15. After that, we estimated the variance in serum protein concentrations that could have been explained by psychiatric medications and discovered that some case-control associations might have been driven by psychiatric medications. In post-hoc analyses, the serum concentration of MMP-7 was found to be positively associated with serum lithium concentration, the duration of lithium therapy, and inversely associated with estimated glomerular filtration rate in an interaction with lithium. The interaction between lithium use and MMP-7 explained the most variance.

Keywords: Serum • Biomarkers • Lithium • Glomerular

Introduction

This is significant because MMP-7 has been suggested to act as a mediator of renal tubulointerstitial fibrosis, a hallmark of lithium-induced nephropathy. Finally, the classification performance of the studied biomarkers was evaluated using machine learning; however, the average performance in unseen data was fair to moderate (area under the receiver operating curve = 0.72). A biomarker for lithium-induced nephropathy and novel insights into the etiopathology of bipolar disorder are provided by our serum biomarker findings.

A RA diagnosis model was developed by identifying 26 metabolites and lipids from the discovery cohort. After that, a validation set was used to test the model, and it came out with an accuracy of 90.2%, sensitivity of 89.7%, and specificity of 90.6%. Using this model, both seropositive and seronegative patients were identified. Six modules of a co-occurrence network constructed with serum omics profiles were found to have a significant association between abnormal energy, lipid, and amino acid metabolism, as well as inflammation and immune activity markers. The RA disease activity was positively correlated with acyl carnitines, aspartyl-phenylalanine, pipecolic acid, phosphatidylethanolamine, and lysophosphatidylethanolamine LPE, whereas the RA disease activity was negatively correlated with histidine and phosphatidic acid [1].

Description

Optically or ultrasonographic methods can be used to directly detect dermal and superficial neurofibromas, whereas PNF and MPNST are frequently diagnosed only after clinical symptoms appear. Whole-body magnetic resonance imaging (MRI) analysis of the internal tumor load of NF1 patients suggests a link between the risk of MPNST development and internal PNF tumor load. However, these imaging methods cannot be used as a standard screening tool. The assumption that overexpression of proteins in PNF and MPNST eventually results in increased systemic concentrations has largely served as the basis for the search for surrogate biomarkers for prompt identification of patients at risk for malignant transformation. In a group of 39 patients with NF1, serum levels of midline and stem cell factor were found to be significantly elevated, but there was no correlation with tumor load or MPNST. We have recently discovered melanoma-inhibitory activity MIA; also referred to as cartilage-derived retinoic acid-sensitive protein was used as a marker for the internal tumor load in a group of 42 NF1 patients. A biomarker for malignant neuroectotermal tumors was previously demonstrated to be MIA. 92 genes encoding putative secreted proteins in MPNST and neurofibromas were looked at for their potential as serum markers in another study. Only adrenomedullin (ADM) was found to be differentially expressed and elevated in the serum of patients with NF1, and a small number of patients with MPNST (n = 5) had even higher serum concentrations [2-4].

The strongest correlation was found between rs150248456 and YKL-40 among immune biomarkers in CSF. On the chromosome,is situated within an intron of CNTNAP5, or contactin-associated protein.The neurexin family includes the CNTNAP5 product. SNPs in CNTNAP5 have been found to be significantly linked to mathematical ability, self-reported educational attainment, cognitive performance, and antipsychotic treatment response in schizophrenia, which is interesting. In this region, two GWS SNPs were found, but only in genotyping waves with control subjects. Even though the concentration of YKL-40 in the CSF of controls and bipolar patients differ, genes are likely to regulate the expression of biomarkers in both groups in a similar way. Intriguingly, a previous GWAS of people with bipolar disorder in Norway, which was replicated in Icelandic samples, also found markers in this gene area that were marginally significant (P 0.05) [5].

We decided to create a cross-flow centrifugal microfluidic platform that is compatible with the biochemistry of amphiphilic biomarkers for the separation of serum from whole blood based on these observations. While this is not the first time a cross-flow filtration technique has been incorporated into a centrifugal microfluidic chip, it is the first to specifically preserve serum-bound amphiphilic molecules.All samples were subjected to cell counts to verify that the design was optimized to purify serum to commercial standards. Testing samples from the device on our waveguide-based optical biosensor for the retention of amphiphilic biomarkers of interest confirmed that the materials used to construct the centrifugal platform were compatible with

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Received: 02 December, 2022, Manuscript No. jmbd-23-89566; **Editor Assigned:** 05 December, 2022, PreQC No. P-89566; **Reviewed:** 18 December, 2022, QC No. Q-89566; **Revised:** 23 December, 2022, Manuscript No. R-89566; **Published:** 30 December, 2022, DOI: 10.37421/2155-9929.2022.13.555

our sample processing criteria. For our biosensing assays, this development makes sample processing much simpler and makes it easier to switch to these technologies when they're needed. Additionally, this technique can be quickly and inexpensively applied to other detection methods that require the separation and preservation of serum from whole blood, even in settings with limited resources

Conclusion

The novel locus in the gene EYS was the top significant region in cases of bipolar disorder associated with CSF YKL-40. Mathematical ability, self-reported educational attainment, body mass index (BMI), alcohol consumption, systolic blood pressure, mood disorder, unipolar depression, and schizophrenia were also found to be significantly correlated with SNPs in EYS. MCP-1 was found to be significantly associated with several SNPs near LINC01288 and EDEM3. EDEM3 was found to be associated with educational attainment, mathematical ability, systemic lupus erythematosus, and cognitive performance, while LINC01288 was found to be significantly associated with BMI. CSF sCD14 concentration was found to be correlated with four GWS SNPs in C8orf37-AS1. C8orf37-AS1 has previously been linked to smoking habits and heel bone mineral density.

Acknowledgement

None.

Conflict of Interest

There are no conflicts of interest by author.

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How to cite this article: Göteson, Andreas. "Serum-based Stability of Circulating MicroRNAs." J Mol Biomark Diagn 13 (2022): 555.